EMERGENCY CASEBOOK

# Case of the month: ''Oh! Drat!—A case of transcutaneous superwarfarin poisoning and its recurrent presentation''

**Simon Binks, Phil Davies**

*Emerg Med J* 2007;**24**:307–308. doi: 10.1136/emj.2006.044925

Superwarfarin poisoning is considered a significant public health problem in the US. In 2004, there were 16 054 cases of poisoning; most were accidental ingestions of rat bait by children but 4576 patients required hospital treatment, 23 patients had major adverse outcomes and 1 patient died. Similar information is unavailable for the UK. The National Poisons Information Service is presently auditing cases.

The case of a farmer who presented with haematuria, 9 days after spilling a rodenticide containing a superwarfarin over himself is reported here. He was physically well except for mild abdominal tenderness. He had grossly deranged clotting studies (prothrombin time (PT) >200 s, activated partial thromboplastin time (APTT) 56 s) that were rapidly corrected with fresh frozen plasma and vitamin K. He was sent home after 5 days without follow up. Unfortunately, he presented again 2 days later, again with haematuria and an international normalised ratio (INR) >10. He required inpatient treatment with high-dose vitamin K for 1 week. Upon discharge, he required daily vitamin K and INR monitoring for a further month. The original inpatient team had not identified the specific poison (chlorophacinone). They were unaware that superwarfarins are more potent and longer acting than warfarin, with toxic effects for weeks or even months, and that large doses of vitamin K are often required.

## CASE REPORT

A 57-year-old small holder presented to our emergency department with a 2-day history of bilateral loin pain and frank haematuria. Nine days earlier, he had accidentally spilt approximately 250 ml of concentrated liquid rat poison over his torso and arms. He had immediately removed his clothes and washed with a hose pipe. He denied ingesting any of the poison. There was no significant or relevant medical history.

On examination, he looked well, was not jaundiced and had no signs of chronic liver disease. He was haemodynamically normal and had mild peri-umbilical tenderness on abdominal examination. Urine dipstick analysis showed blood 4+. His full blood count, renal and liver function tests were normal. His coagulation screen, however, was grossly abnormal, with a prothrombin time (PT) greater than 200 s (normal range 11–14 s) and an activated partial thromboplastin time (APTT) of 56 s (normal range 23–32 s) with a normal fibrinogen.

A diagnosis of accidental poisoning with a warfarin-like substance was made although the exact constituents of the poison were not determined at this stage. He was treated with fresh frozen plasma (4 U) and vitamin K (20 mg intravenously). His clotting abnormalities were rapidly corrected such that the following day his PT was 19 s and his APTT 33 s. However, within 2 days his PT was >200 s. He was treated with further doses of vitamin K intravenously and with a PT of 20 s. On day five of his admission, he was discharged home.

Unfortunately, he presented again 2 days later, again with frank haematuria. His clotting studies were again grossly abnormal, with an INR >10. He was admitted and further given vitamin K. A haematology review and information from a relative of the patient (a veterinarian) confirmed that the poison involved was a superwarfarin (specifically, ''Drat'' containing 0.25% chlorophacinone), which explained the longevity of its effect. The patient remained in hospital for the following week, requiring vitamin K 20 mg daily. After discharge, he required vitamin K 20–30 mg daily and INR monitoring every alternate day for a further month.

## DISCUSSION

Warfarin was first identified by Karl Link in 1933 as the active component of mouldy sweet clover that caused haemorrhagic disease in cattle. It has since been used as a rodenticide. However, increasing resistance in rats has led to the development and use of the superwarfarins (derivatives of 4-hydroxy coumarin such as difenacoum, bromadiolone and brodifacoum, and indanedione derivatives such as chlorophacinone, pindone and diphacinone). The superwarfarins are more potent and much longer acting than warfarin. The plasma half-life of warfarin is 17 h in rats, whereas that of brodifacoum is 156 h.[1] The pharmacokinetics of the superwarfarins in humans is unknown. Coumarin and its derivatives cause a bleeding diathesis by inhibiting hepatic synthesis of the vitamin K-dependent coagulation factors II, VII, IX and X.

In the US, superwarfarins have been described as a significant public health problem.[2] In 2004, there were 16 054 cases of superwarfarin poisoning or exposure.[2] The majority were accidental ingestions of rat bait by children; 4576 patients required treatment in hospital, 23 patients had major adverse outcomes and 1 patient died. Similar information is currently unavailable in the UK, and the National Poisons Information Service is auditing suspected cases.

Toxicity of superwarfarins absorbed through skin contact is very unusual but has been reported previously.[3] Little is known about this route of absorption in humans. As in our case, haematuria is a common feature of poisoning via skin absorption or ingestion, although bruising, epistaxis and bleeding gums are also frequent. Patients may present with more severe complications, and intracranial haemorrhage after cutaneous exposure has been described.[3]

Typically patients have deranged coagulation studies with both PT and APTT prolongation. These abnormalities can be corrected in the laboratory by the addition of normal serum to the patients' sample suggesting factor deficiency. Assays of vitamin K-dependent factors are low. Specific titres for superwarfarin have been measured in cases where a history of

**Abbreviations:** APTT, activated partial thromboplastin time; INR, international normalized ratio; PT, prothrombin time

**Key points**

- Superwarfarins may have toxic effects for weeks or even months.
- Toxic doses can be absorbed transcutaneously.
- High doses of Vitamin K are often required in treatment.
- Long term follow-up is required.

poisoning is unknown or withheld. Intentional poisoning as part of Munchausen's syndrome should be considered.[1]

Patients with severe haemorrhage will require correction of their coagulopathy with fresh frozen plasma and vitamin K. In the absence of severe haemorrhage but abnormal clotting, vitamin K alone can be used. It should be given initially intravenously, and will be required in much higher doses (up to 125 mg/day) than in warfarin toxicity.[4] Long-term oral vitamin K therapy and monitoring is necessary to avoid recurrence of symptoms and representation as in our case.

**Authors' affiliations**
**Simon Binks, Phil Davies,** Emergency Department, Cheltenham General Hospital, Cheltenham, UK

Competing interests: None.

Informed consent was obtained for publication of this report.

Correspondence to: S Binks, Emergency Department, Cheltenham General Hospital, Cheltenham GL53 7AN, UK; simon_binks@hotmail.com

Accepted 5 December 2006

## REFERENCES

1 **Tecimer C**, Yam LT. Surreptitious superwarfarin poisoning with brodifacoum. *South Med J* 1997;**90**:1053–5.
2 **Chua JD**, Friedenberg WR. Superwarfarin poisoning. *Arch Int Med* 1998;**158**:1929–32.
3 **Abell TL**, Merigan KS, Lee JM, *et al*. Cutaneous exposure to Warfarin-like anticoagulant causing an intracerebral haemorrhage: a case report. *Clin Toxicol* 1994;**32**:69–73.
4 **Watson WA**, Litovitz TL, Rodgers GC, *et al*. 2004 Annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med* 2005;**23**:589–666.

# IMAGES IN EMERGENCY MEDICINE

## Pituitary apoplexy can mimic subarachnoid haemorrhage clinically and radiologically

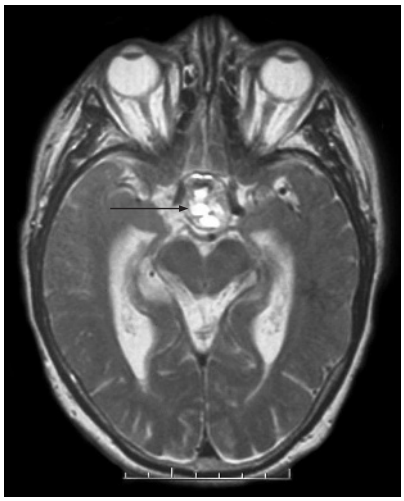

**Figure 1** T2-weighted axial magnetic resonance imaging scan showing a lesion in the pituitary fossa (arrow), displaying heterogeneous signal intensity suggesting recent apoplexy.

A 74-year-old man presented with a sudden onset headache, collapse, neck stiffness and photophobia. Extensive subarachnoid haemorrhage (SAH) with hydrocephalus was diagnosed on computed tomography. Negative cerebral artery angiography was carried out two times before he was discharged home 3 weeks later, having made a full recovery. About 15% of patients with SAH have no discernable cause of bleeding on angiography or other neuroimaging.[1]

The patient was readmitted 8 months later with headaches and a gradual onset of bitemporal hemianopia. A magnetic resonance imaging scan showed a pituitary tumour (fig 1), and arrangements were made for urgent surgery. The day before his surgery, his condition deteriorated acutely, he complained of headache and nausea and was barely able to perceive light in either eye. He underwent emergency trans-sphenoidal hypophysectomy.

The presence of any visual disturbance (particularly of a bitemporal distribution) in conjunction with a sudden-onset headache is an important clinical pointer to the diagnosis of pituitary apoplexy rather than SAH.

**I G Sergides**
King's College Hospital, London, UK
**P S Minhas**
**N Anotun**
**J D Pickard**
Addenbrookes Hospital, Cambridge, UK

Correspondence to: I Sergides, King's College Hospital, Denmark Hill, London SE5 9RS, UK; ysergides@hotmail.com

doi: 10.1136/emj.2006.036616

Accepted for publication 3 April 2006

## REFERENCE

1 **Flaherty ML**, Haverbusch M, Kissela B, *et al*. Perimesencephalic subarachnoid hemorrhage: incidence, risk factors, and outcome. *J Stroke Cerebrovasc Dis* 2005;**14**:267–71.